PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WIBBELMANN, Jobst
Wuesthoff & Wuesthoff
Schweigerstrasse 2
D-81541 München
ALLEMAGNE

Date of mailing (day/month/year)
04 April 2001 (04.04.01)

Applicant's or agent's file reference
EP-83244/PCT

IMPORTANT NOTIFICATION

International application No.
PCT/EP99/06830

International filing date (day/month/year)
15 September 1999 (15.09.99)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address
GOLDHAM BIOGLAN PHARMA GMBH
Am Wasserberg 11
D-86441 Zusmarshausen
Germany

State of Nationality: DE
State of Residence: DE
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [X] the name [X] the address [X] the nationality [X] the residence

Name and Address
OMNIA PHARMA S.R.L.
Via Fiume Giallo 228
I-00144 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
Céline Faust
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 12 May 2000 (12.05.00)	
International application No. PCT/EP99/06830	**Applicant's or agent's file reference** EP-83244/PCT
International filing date (day/month/year) 15 September 1999 (15.09.99)	**Priority date** (day/month/year) 16 September 1998 (16.09.98)
Applicant FRANK, Artur et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

10 April 2000 (10.04.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Nestor Santesso

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WIBBELMANN, Jobst
Wuesthoff & Wuesthoff
Schweigerstrasse 2
D-81541 München
ALLEMAGNE

Date of mailing (day/month/year)
25 May 2000 (25.05.00)

Applicant's or agent's file reference
EP-83244/PCT

IMPORTANT NOTIFICATION

International application No.
PCT/EP99/06830

International filing date (day/month/year)
15 September 1999 (15.09.99)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
GIANETTINO, Andreina
Via Francesco Sapori, 49
I-00143 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [X] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address
GIANNETTINO, Andreina
Via Francesco Sapori, 49
I-00143 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
A. Karkachi
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WIBBELMANN, Jobst
Wuesthoff & Wuesthoff
Schweigerstrasse 2
D-81541 München
ALLEMAGNE

Date of mailing (day/month/year)
13 March 2001 (13.03.01)

Applicant's or agent's file reference
EP-83244/PCT

IMPORTANT NOTIFICATION

International application No.
PCT/EP99/06830

International filing date (day/month/year)
15 September 1999 (15.09.99)

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address
GOLDHAM BIOGLAN PHARMA GMBH
Am Wasserberg 11
D-86441 Zusmarshausen
Germany

State of Nationality: DE
State of Residence: DE
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [X] the name [X] the address [X] the nationality [X] the residence

Name and Address
OMNIA PHARMA S.R.L.
Via Fiume Giallo 228
I-00143 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Dorothée Mülhausen

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WIBBELMANN, Jobst
Wuesthoff & Wuesthoff
Schweigerstrasse 2
D-81541 München
ALLEMAGNE

Date of mailing (day/month/year)
13 March 2001 (13.03.01)

Applicant's or agent's file reference
EP-83244/PCT

IMPORTANT NOTIFICATION

International application No.
PCT/EP99/06830

International filing date (day/month/year)
15 September 1999 (15.09.99)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
GIANNETTINO, Andreina
Via Francesco Sapori, 49
I-00143 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
GIANNETTINO, Andreina
Via Fiume Giallo 228
I-00143 Roma
Italy

State of Nationality: IT
State of Residence: IT
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

Authorized officer
Dorothée Mülhausen
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WIBBELMANN, Jobst
Wuesthoff & Wuesthoff
Schweigerstrasse 2
D-81541 München
ALLEMAGNE

Date of mailing (day/month/year) 04 April 2001 (04.04.01)	
Applicant's or agent's file reference EP-83244/PCT	**IMPORTANT NOTIFICATION**
International application No. PCT/EP99/06830	**International filing date** (day/month/year) 15 September 1999 (15.09.99)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
GIANNETTINO, Andreina Via Francesco Sapori, 49 I-00143 Roma Italy	IT	IT
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
GIANNETTINO, Andreina Via Fiume Giallo 228 I-00143 Roma Italy	IT	IT
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Céline Faust
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61K 49/04

A3

(11) International Publication Number: WO 00/15266

(43) International Publication Date: 23 March 2000 (23.03.00)

(21) International Application Number: PCT/EP99/06830

(22) International Filing Date: 15 September 1999 (15.09.99)

(30) Priority Data:
98117598.7 16 September 1998 (16.09.98) EP

(71) Applicant *(for all designated States except US)*: GOLDHAM BIOGLAN PHARMA GMBH [DE/DE]; Am Wasserberg 11, D–86441 Zusmarshausen (DE).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: FRANK, Artur [DE/DE]; Am Wasserberg 11, D–86441 Zusmarshausen (DE). GIANETTINO, Andreina [IT/IT]; Via Francesco Sapori, 49, I–00143 Roma (IT).

(74) Agent: WIBBELMANN, Jobst; Wuesthoff & Wuesthoff, Schweigerstrasse 2, D–81541 München (DE).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(88) Date of publication of the international search report:
25 May 2000 (25.05.00)

(54) Title: RADIO–CONTRAST AGENTS

(57) Abstract

An imaging or contrast agent comprising a stereoisomer of a compound with at least one chiral centre, wherein said stereoisomer is in stereoisomeric excess and causes fewer adverse side effects on administration, or is less chemotoxic, than at least one other stereoisomer of said chiral compound.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

[redacted] Application No
PCT/EP 99/06830

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K49/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FELDER E ET AL: "IOPAMIDOL" 1 January 1988 (1988-01-01) , ANALYTICAL PROFILES OF DRUG SUBSTANCES, VOL. 17, PAGE(S) 115 - 154 XP000562617 the whole document	1-8,12, 13
X	WO 97 02235 A (RECORDATI CHEM PHARM ;TARQUINI ANTONIO (IT); DONNARUMMA MARIA (IT)) 23 January 1997 (1997-01-23) the whole document	1-8,12, 13
X	WO 98 34908 A (DESANTIS NICOLA ;BRACCO INT BV (NL)) 13 August 1998 (1998-08-13) the whole document	1-8,12, 13

-/—

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 February 2000	15/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Veronese, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

[redacted]nal Application No
PCT/EP 99/06830

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	DAWSON, PETER ET AL.: "Isomeric Purity and Supersaturation of Iopamidol" BR. J. RADIOL., vol. 56, no. 670, 1983, pages 711-713, XP002096202 the whole document	1-14
X	PITRE D. ET AL.: "Development, Chemistry and Physical Properties of Iopamidol and its Analogs" INVESTIGATIVE RADIOLOGY, vol. 15, no. 6 Suppl., 1980, pages S301-S306, XP002096203 the whole document	1-14
X	WO 97 19705 A (ELMALEH DAVID R) 5 June 1997 (1997-06-05) the whole document	1-7
A	THE MERK LAORATORIES: "The Merk Index" , MERK AND CO. INC. , N.J. (U.S.A.) XP002131835 page 862 page 866-869	12

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/06830

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9702235 A	23-01-1997	IT MI951429 A	07-01-1997
		IT MI952572 A	06-06-1997
		AU 6516196 A	05-02-1997
		EP 0842141 A	20-05-1998
WO 9834908 A	13-08-1998	AU 1455397 A	26-08-1998
		EP 0966428 A	29-12-1999
		NO 993851 A	10-08-1999
		ZA 9801070 A	27-08-1998
WO 9719705 A	05-06-1997	CA 2238860 A	05-06-1997
		EP 0869821 A	14-10-1998

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
EP-83244/PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/06830	15/09/1999	16/09/1998
International Patent Classification (IPC) or national classification and IPC A61K49/00		
Applicant GOLDHAM BIOGLAN PHARMA GMBH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/04/2000	21.12.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Simm, M.D. Telephone No. +49 89 2399 7411

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/06830

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-5	as originally filed				

Claims, No.:

1-4	as received on	10/04/2000	with letter of	10/04/2000	

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3.

because:

☒ the said international application, or the said claims Nos. 3, in respect of i.a. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-4
Industrial applicability (IA)	Yes:	Claims	

No: Claims 3

2. Citations and explanations
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 3 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: DAWSON, PETER ET AL.: 'Isomeric Purity and Supersaturation of Iopamidol' BR. J. RADIOL., vol. 56, no. 670, 1983, pages 711-713

D2: FELDER E ET AL: 'IOPAMIDOL' 1 January 1988 (1988-01-01) , ANALYTICAL PROFILES OF DRUG SUBSTANCES, VOL. 17, PAGE(S) 115 - 154

Novelty and Inventive Step (Art. 33(2) and 33(3) PCT).

D1 discloses that the solubility of iopamidol probably depends on the isomeric purity of the preparation, being for instance the solubility of the L(S)-form higher than the racemate's one. A typical D(R)-isomer concentration is 1.6% (see page 713, left column, second paragraph). The document neither mentions a solution of iopamidol with a concentration of R-iopamidol higher than 50% nor discloses the relationship between R-iopamidol and fewer adverse side effects on administration (chemotoxicity).

According to the remaining prior art and as stated in the description of the present application iopamidol is only available in the S-form (98.9% of L(S)-form and 1.62 %of D(R)-form) (see D2, 3.3.1 optical rotation).

Thus, the subject-matter of claims 1-4 appears to be novel.

However, the present invention does not involve an inventive step. The technical problem to be solved in view of the prior art which uses S (L)-iopamidol as an imaging or contrast agent is to reduce the chemotoxicity of the compound. The solution of choosing the R (D)-isomer is obvious taking into accoount that biological systems depen on specific detailed recognition of molecules involving differentiation between quiral forms and that all amino acids in the proteins have the L-configuration. Therefore, if the objective is to reduce chemotoxicity, namely to avoid interaction with molecules as proteins in the body, it is obvious to use the R (D)-isomer of the compound.

Industrial Applicability (Art. 33(4) PCT).

For the assessment of the present claim 3 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Amended claims

1. An imaging or contrast agent comprising iopamidol characterised in that said agent comprises greater than 50 % of R-iopamidol.

2. The imaging or contrast agent as claimed in claim 1, wherein said agent comprises greater than 80 % R-iopamidol.

3. A use of R-iopamidol in an imaging or contrast agent wherein said agent causes fewer adverse side effects on administration.

4. A use of R-iopamidol to produce an imaging or contrast agent being less chemotoxic.

9573

15

REC'D 29 JAN 2001
WIPO
PCT

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
EP-83244/PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/06830	15/09/1999	16/09/1998
International Patent Classification (IPC) or national classification and IPC A61K49/00		
Applicant GOLDHAM BIOGLAN PHARMA GMBH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items: CORRECTED VERSION

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/04/2000	25. 01. 01
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Simm, M.D. Telephone No. +49 89 2399 7411

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/06830

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-5	as originally filed				

Claims, No.:

1-4	as received on	10/04/2000	with letter of	10/04/2000	

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3.

because:

☒ the said international application, or the said claims Nos. 3, in respect of i.a. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-2
	No:	Claims	3-4
Inventive step (IS)	Yes:	Claims	1-2
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1,2,4

No: Claims 3

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R Item I

Basis of the report

D1: DAWSON, PETER ET AL.: 'Isomeric Purity and Supersaturation of Iopamidol' BR. J. RADIOL., vol. 56, no. 670, 1983, pages 711-713

D2: FELDER E ET AL: 'IOPAMIDOL' 1 January 1988 (1988-01-01) , ANALYTICAL PROFILES OF DRUG SUBSTANCES, VOL. 17, PAGE(S) 115 - 154

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 3 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty (Art. 33(2) PCT).

D1 discloses that the solubility of iopamidol probably depends on the isomeric purity of the preparation, being for instance the solubility of the L(S)-form higher as the racemate's one. A typical D(R)-isomer concentration is 1.6% (see page 713, left column, second paragraph). The document neither mentions a solution of iopamidol with a concentration of R-iopamidol higher than 50% nor discloses the relationship between R-iopamidol and fewer adverse side effects on administration (chemotoxicity).

According to the remaining prior art and as stated in the description of the present application iopamidol is only available in the S-form (98.9% of L(S)-form and 1.62 %of

D(R)-form) (see D2, 3.3.1 optical rotation). Thus, the subject-matter of claims 1-2 appears to be novel.

However, the subject-matter of claims 3 and 4 which refers to the use of R-iopamidol without indicating the % is not considered to be novel because the contrast agents known from the prior art comprise R-iopamidol (1.6 %) and the expressions "being less chemotoxic" and "wherein said agent causes fewer adverse side effects on administration" have no limiting effect over the scope of these claims (see Item VIII).

Inventive Step (Art. 33(3) PCT).

The present invention differs from the cited prior art in that the contrast agent comprises more than 50% R-iopamidol. The technical effect is that the contrast agent is less chemotoxic. The technical problem solved by the present application is then to provide a contrast agent based on iopamidol which is less chemotoxic.
The solution given in the present invention, a contrast agent comprising more than 50% R-iopamidol is neither disclosed nor merely suggested in the cited prior art. Thus, the subject-matter of claims 1-2 appears to be inventive.

Industrial Applicability (Art. 33(4) PCT).

For the assessment of the present claim 3 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Item VIII
Certain observations on the international application

Claims 3 and 4 appear to lack an essential feature according to the description (see page 2, lines 25-30) and the subject-matter of claim 1, namely that the contrast agent comprises more that 50% of R-iopamidol (Art. 6 and PCT Guidelines III-4.3).

Moreover, the expressions "wherein said agent causes fewer adverse side effects on administration" in claim 3 and "being less chemotoxic" in claim 4 express just a result to be achieved and as such render the scope of these claims unclear (Art. 6 and PCT Guidelines III-4).

In claim 1 it appears that the expression "greater than" should read "more than".

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Wibbelmann, Jobst
WUESTHOFF & WUESTHOFF
Schweigerstrasse 2
81541 München
ALLEMAGNE

WUESTHOFF & WUESTHOFF
PATENT- UND RECHTSANWÄLTE
26. JAN. 2001

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	25. 01. 01
Applicant's or agent's file reference	IMPORTANT NOTIFICATION
EP-83244/PCT	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/06830	15/09/1999	16/09/1998

Applicant
GOLDHAM BIOGLAN PHARMA GMBH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Senkel, H Tel.+49 89 2399-8071

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
EP-83244/PCT		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/06830	15/09/1999	16/09/1998

International Patent Classification (IPC) or national classification and IPC
A61K49/00

Applicant
GOLDHAM BIOGLAN PHARMA GMBH et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/04/2000	25. 01. 01

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Simm, M.D.

Telephone No. +49 89 2399 7411

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/06830

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-5	as originally filed				

Claims, No.:

1-4	as received on	10/04/2000	with letter of	10/04/2000	

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 3.

because:

☒ the said international application, or the said claims Nos. 3, in respect of i.a. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-2
	No:	Claims	3-4
Inventive step (IS)	Yes:	Claims	1-2
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1,2,4

No: Claims 3

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of the report

D1: DAWSON, PETER ET AL.: 'Isomeric Purity and Supersaturation of Iopamidol' BR. J. RADIOL., vol. 56, no. 670, 1983, pages 711-713

D2: FELDER E ET AL: 'IOPAMIDOL' 1 January 1988 (1988-01-01) , ANALYTICAL PROFILES OF DRUG SUBSTANCES, VOL. 17, PAGE(S) 115 - 154

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 3 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty (Art. 33(2) PCT).

D1 discloses that the solubility of iopamidol probably depends on the isomeric purity of the preparation, being for instance the solubility of the L(S)-form higher as the racemate's one. A typical D(R)-isomer concentration is 1.6% (see page 713, left column, second paragraph). The document neither mentions a solution of iopamidol with a concentration of R-iopamidol higher than 50% nor discloses the relationship between R-iopamidol and fewer adverse side effects on administration (chemotoxicity).

According to the remaining prior art and as stated in the description of the present application iopamidol is only available in the S-form (98.9% of L(S)-form and 1.62 %of

D(R)-form) (see D2, 3.3.1 optical rotation). Thus, the subject-matter of claims 1-2 appears to be novel.

However, the subject-matter of claims 3 and 4 which refers to the use of R-iopamidol without indicating the % is not considered to be novel because the contrast agents known from the prior art comprise R-iopamidol (1.6 %) and the expressions "being less chemotoxic" and "wherein said agent causes fewer adverse side effects on administration" have no limiting effect over the scope of these claims (see Item VIII).

Inventive Step (Art. 33(3) PCT).

The present invention differs from the cited prior art in that the contrast agent comprises more than 50% R-iopamidol. The technical effect is that the contrast agent is less chemotoxic. The technical problem solved by the present application is then to provide a contrast agent based on iopamidol which is less chemotoxic.
The solution given in the present invention, a contrast agent comprising more than 50% R-iopamidol is neither disclosed nor merely suggested in the cited prior art. Thus, the subject-matter of claims 1-2 appears to be inventive.

Industrial Applicability (Art. 33(4) PCT).

For the assessment of the present claim 3 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Item VIII
Certain observations on the international application

Claims 3 and 4 appear to lack an essential feature according to the description (see page 2, lines 25-30) and the subject-matter of claim 1, namely that the contrast agent comprises more that 50% of R-iopamidol (Art. 6 and PCT Guidelines III-4.3).

Moreover, the expressions "wherein said agent causes fewer adverse side effects on administration" in claim 3 and "being less chemotoxic" in claim 4 express just a result to be achieved and as such render the scope of these claims unclear (Art. 6 and PCT Guidelines III-4).

In claim 1 it appears that the expression "greater than" should read "more than".

Amended claims

1. An imaging or contrast agent comprising iopamidol characterised in that said agent comprises greater than 50 % of R-iopamidol.

2. The imaging or contrast agent as claimed in claim 1, wherein said agent comprises greater than 80 % R-iopamidol.

3. A use of R-iopamidol in an imaging or contrast agent wherein said agent causes fewer adverse side effects on administration.

4. A use of R-iopamidol to produce an imaging or contrast agent being less chemotoxic.

9573

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
EP-83244/PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 99/ 06830	15/09/1999	16/09/1998
Applicant		
GOLDHAM BIOGLAN PHARMA GMBH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with th abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes th invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/06830

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K49/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FELDER E ET AL: "IOPAMIDOL" 1 January 1988 (1988-01-01) , ANALYTICAL PROFILES OF DRUG SUBSTANCES, VOL. 17, PAGE(S) 115 - 154 XP000562617 the whole document	1-8,12, 13
X	WO 97 02235 A (RECORDATI CHEM PHARM ;TARQUINI ANTONIO (IT); DONNARUMMA MARIA (IT)) 23 January 1997 (1997-01-23) the whole document	1-8,12, 13
X	WO 98 34908 A (DESANTIS NICOLA ;BRACCO INT BV (NL)) 13 August 1998 (1998-08-13) the whole document	1-8,12, 13

-/—

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 February 2000	15/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Veronese, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/06830

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAWSON, PETER ET AL.: "Isomeric Purity and Supersaturation of Iopamidol" BR. J. RADIOL., vol. 56, no. 670, 1983, pages 711-713, XP002096202 the whole document	1-14
X	PITRE D. ET AL.: "Development, Chemistry and Physical Properties of Iopamidol and its Analogs" INVESTIGATIVE RADIOLOGY, vol. 15, no. 6 Suppl., 1980, pages S301-S306, XP002096203 the whole document	1-14
X	WO 97 19705 A (ELMALEH DAVID R) 5 June 1997 (1997-06-05) the whole document	1-7
A	THE MERK LAORATORIES: "The Merk Index" , MERK AND CO. INC. , N.J. (U.S.A.) XP002131835 page 862 page 866-869	12

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/06830

Patent document cited in search report	Publication dat	Patent family member(s)	Publication date
WO 9702235 A	23-01-1997	IT MI951429 A	07-01-1997
		IT MI952572 A	06-06-1997
		AU 6516196 A	05-02-1997
		EP 0842141 A	20-05-1998
WO 9834908 A	13-08-1998	AU 1455397 A	26-08-1998
		EP 0966428 A	29-12-1999
		NO 993851 A	10-08-1999
		ZA 9801070 A	27-08-1998
WO 9719705 A	05-06-1997	CA 2238860 A	05-06-1997
		EP 0869821 A	14-10-1998